Atty Dkt. No.: UCAL-222 USSN: 10/017,718

IN THE CLAIMS

Cancel claims 9-13 and 16-19 without prejudice to renewal.

Please enter new claim 23, as shown below.

1. (Previously presented) A gene-targeted mouse comprising a modified endogenous apolipoprotein E (apoE) allele, wherein said modified allele comprises an apoE-encoding nucleic acid under transcriptional control of endogenous regulatory sequences, wherein the modified allele encodes a modified apoE polypeptide that exhibits domain interaction characteristic of human apolipoprotein E4 (apoE4), wherein the modified apoE polypeptide comprises a Thr → Arg substitution at a position equivalent to amino acid 61 of human apoE4, and wherein the modified apoE polypeptide exhibits preferential binding to lower density lipoproteins.

I. AMENDMENTS

- 2. (Canceled)
- 3. (Previously presented) The gene-targeted mouse of claim 1, wherein the gene-targeted mouse is homozygous for the modified apoE allele.
 - 4. (Canceled)
- 5. (Previously presented) A cell isolated from the gene-targeted mouse of claim 1, wherein said cell produces the modified apoE polypeptide.
 - 6. (Canceled)
- 7. (Previously presented) The cell of claim 5, wherein the cell is homozygous for the modified apoE allele.
 - 8.-13. (Canceled)

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14. (Previously presented) A method of identifying an agent that reduces a phenomenon associated with Alzheimer's disease (AD), the method comprising:

- a) contacting the gene-targeted mouse of claim 1 with a test agent; and
- b) determining the effect of the test agent on reducing a phenomenon associated with AD.
- 15. (Previously presented) The method of claim 14, wherein the phenomenon associated with AD is selected from the group consisting of amyloid deposits, neuronal cell loss, and neurofibrillary tangles.

16.-19. (Canceled)

- 20. (Previously presented) The cell according to claim 5, wherein said cell is an astrocyte.
- 21. (Previously presented) The cell according to claim 5, wherein said cell is a microglial cell.
- 22. (Previously presented) The cell according to claim 5, wherein the cell is a neuronal cell.
- 23. (New) The gene-targeted mouse of claim 1, wherein the mouse exhibits apoE4-related neurodegeneration.